

Applicant: Mercy M. Davidson  
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**REMARKS**

Claims 1, 3-5, 8, 9, and 12 are pending in the subject application. Claims 3-5, 8, 9, and 12 are allowed. Applicant has hereinabove amended claim 1. Accordingly, upon entry of this Amendment, claims 1, 3-5, 8, 9, and 12 will still be pending and claim 1 will still be under examination.

Support for the amendments to claim 1 is found, *inter alia*, in the specification as follows: page 19, line 30 to page 20, line 6; page 22, lines 17-35; page 20, lines 15-23; and page 23, lines 9-13.

Applicant maintains that these amendments to claim 1 do not raise any issue of new matter, and that claim 1, as amended, is fully supported by the specification as originally filed.

**January 18, 2005 Examiner's Interview, January 19, 2005 Second Preliminary Amendment, and March 15, 2005 and March 30, 2005 Telephone Conferences**

On January 18, 2005, applicant's undersigned attorney, Alan J. Morrison, Esq. had a telephonic interview with Examiner Richard Schnizer concerning applicant's Preliminary Amendment filed on November 12, 2004 with the United States Patent and Trademark Office. Applicant wishes to thank the Examiner for his time and consideration during the interview.

During the January 18, 2005 interview, the Examiner and Mr. Morrison agreed that claim 1, as amended herein, would be in condition for allowance. Further, applicant

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understood that claims 3-5 would be in condition for allowance upon entry of the Preliminary Amendment, and claims 8, 9 and 12 were already allowed. Applicants again note that at present, claims 3-5, 8, 9, and 12 are allowed.

Applicant filed a January 19, 2005 Second Preliminary Amendment Regarding Examiner's Interview ("Second Preliminary Amendment") via facsimile with the Patent Office which included the amendments to claim 1 presented herein. However, during March 15, 2005 and March 30, 2005 telephone conferences between the Examiner and Cindy Yang, Esq. of the undersigned's firm, the Examiner indicated that due to time constraints, he would not review or consider the Second Preliminary Amendment, and suggested that instead, the contents of the Second Preliminary Amendment be incorporated into an Amendment in response to the outstanding January 25, 2005 Office Action.

Accordingly, applicant has incorporated the contents of the Second Preliminary Amendment into this Amendment and looks forward to the issuance of a Notice of Allowance in connection with this application.

**Claim Rejection Under 35 U.S.C. §102(b)**

The Examiner rejected claim 1 under 35 U.S.C. §102(b) as allegedly anticipated by Wang et al. (In Vitro Cellular and Developmental Biology 27(1): 63-74, 1/1991; "Wang").

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In response to the Examiner's rejection, applicant respectfully traverses.

Under 35 U.S.C. §102(b), and as stated in M.P.E.P. §2131.01, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Thus, for Wang to anticipate the cell line of claim 1, it would have to teach each and every element thereof.

Wang fails to do this.

Briefly, claim 1, as amended, provides for an immortalized human undifferentiated cardiomyocyte cell line, wherein the cell line wherein the cell line (a) expresses *β-myosin heavy chain, connexin-43, and desmin*, (b) does not exhibit obvious voltage-activated conductances in whole-cell voltage-clamp recordings, (c) comprises a replicable vector that expresses SV-40 large T antigen, and (d) is produced by a method comprising the step of fusing a post-mitotic primary non-immortalized human cardiomyocyte obtained from adult human heart tissue with a human fibroblast, the fibroblast (i) having been treated with ethidium bromide; (ii) comprising a replicable vector expressing SV40 large T antigen which confers immortality on a cell comprising same; and (iii) being free of mitochondrial DNA.

Wang teaches a human cardiac myocyte cell line ("W1") derived from fetal cardiac tissue. W1 is produced by cotransfecting fetal cardiac myocytes with the plasmids

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pSV2Neo and PRSVTA<sub>g</sub>, using a calcium phosphate procedure. Wang, pages 63 [abstract] and 64. Wang also teaches that its W1 cell line expresses myosin; cardiac myosin; skeletal muscle myosin; cardiac, skeletal, and smooth muscle actin; and SV40 TAg. Wang, page 69 (Table 2). Nowhere does Wang teach an immortalized human undifferentiated cardiomyocyte cell line that expresses  $\beta$ -myosin heavy chain, connexin-43, and desmin, and is derived from post-mitotic primary non-immortalized human cardiomyocytes obtained from adult human heart tissue.

Furthermore, as mentioned in applicant's May 21, 2004 Amendment In Response To January 27, 2004 Office Action, and a May 18, 2004 Declaration of Mercy M. Davidson, Ph.D., the claimed cell line is not the same as the W1 cell line of Wang since the claimed cell line exhibits morphological and doubling time differences relative to the W1 cell line of Wang.

As shown in Exhibit C of the May 18, 2004 Declaration of Mercy M. Davidson, Ph.D., the claimed cell line, as illustrated by AC16 cells (derived from human adult cardiomyocytes) and RL14 cells (derived from human fetal cardiomyocytes), is characterized by homogeneous cells which (a) are evenly-shaped, (b) have large central nuclei and (c) have a larger average ratio of nucleus volume to cytoplasm volume than do native primary human cardiomyocyte cells. Both AC16 cells and RL14 cells are also smaller in size relative to native primary human cardiomyocytes. In contrast to the claimed cell line, the W1 cell line shown in Figures 1 and 5 of Wang contains heterogeneous, refractile, spindle-shaped cells.

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The cells of the W1 cell line morphologically resemble native human primary cardiomyocytes. Wang states that the W1 cell line "has been shown to share morphologic and phenotypic characteristics with native human fetal cardiomyocytes," that W1 cells "look very similar" to native primary cardiomyocytes under light and electron microscopy, and that "by morphologic criteria these two types of cells [W1 cells and human fetal cardiac myocytes] are indistinguishable from one another." Wang, page 73, column 1, ¶1; page 66, column 1, 2<sup>nd</sup> full paragraph; and page 66, legend for Figure 1, respectively.

As shown in Exhibit D of the May 18, 2004 Declaration of Mercy M. Davidson, Ph.D., the claimed cell line has a calculated doubling time of 24.49 hours. In contrast, the W1 cell line of Wang exhibits a doubling time of 55.4 hours. Wang, page 66, column 2, 1<sup>st</sup> full paragraph. This doubling time is more than twice as long as the 24.49 hour doubling time of the claimed cell line.

As demonstrated above, the claimed cell line is not the same as the W1 cell line of Wang, and the Examiner has not established any teaching to the contrary. Therefore, Wang fails to anticipate the cell line of claim 1.

In view of the above remarks, applicant maintains that claim 1 satisfies the requirements of 35 U.S.C. §102(b).

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**Claim Rejection Under 35 U.S.C. §112**

The Examiner rejected claim 1 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner stated that claim 1 as written is interpreted as embracing a broad genus of cells with different structural and functional characteristics. The Examiner also stated that the limitation "undifferentiated cardiomyocyte" receives very little patentable weight because it is unclear what structural and functional characteristics an undifferentiated cell must have in order to be considered an undifferentiated cardiomyocyte. The Examiner further stated that it is unclear how an undifferentiated cardiomyocyte differs from any other undifferentiated cell. The Examiner suggested that claim 1 should be limited to an immortalized undifferentiated cardiomyocyte cell line that expresses SV40 large T antigen,  $\beta$  myosin heavy chain, desmin, and connexin-43.

In response to the Examiner's rejection, without conceding the correctness of the Examiner's position, applicant notes that amended claim 1 contains language which fully addresses the Examiner's stated concern. Thus, the Examiner's rejection of claim 1 is obviated.

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**Summary**

Applicants maintain that claim 1, as amended, is in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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